## SCIENTIFIC ABSTRACT

In a Phase I study in 10 patients with chronic Human Immunodeficiency Virus-l (HIV-l) infection, we have shown the feasibility and safety of infusing autologous CD34+ hematopoietic progenitor cells transduced either with a MoMLV-derived retrovirus (LNL6) or LNL6 containing an anti-HIV-l ribozyme (RRz2). In all patients, the transduced cells contributed to myeloid and lymphoid progeny. In those who received higher numbers of transduced CD34+ cells, this reconstitution was evident for 2.5 years (the most recent time-point assessed). Neither the Phase I trial nor the proposed Phase II trial involves myeloablative therapy. The overall goal of the present study is to determine in patients with chronic HIV-l safety and efficacy of autologous CD34+ cells transduced with RRz2. The ribozyme gene (Rz2) is targeted to a highly conserved region of the HIV genome (the *tat* HIV-I regulatory gene); LNL6 is a benign replication-incompetent retroviral vector. The study will compare two treatment groups: a group whose CD34+ cells are transduced with LNL6, and a group whose CD34+ cells are transduced with RRz2. During the initial reconstitution period following CD34+ cell infusion, the patients are maintained on Anti-Retroviral Therapy (ART). At week 24 post CD34+ infusion, the ART is stopped and an initial 8 week Analytic Treatment Interruption (ATI#l) is begun. This is followed by reintroduction of ART for 12 weeks and then a second Analytic Treatment Interruption (ATI#2). Safety assessments will be made repeatedly throughout the two year protocol and continue on an annual basis thereafter as per FDA/CBER requirements. Efficacy will be determined at the end of ATI#2 (51 & 52 weeks post-infusion) by comparison of viral load in the two treatment groups. Secondary end-points will be CD4+ count, proviral DNA, relative gene marking of progeny cells, time to resume ART and sequence of the *tat* gene in the region targeted by Rz2.